

**Translation**

**PATENT COOPERATION TREATY**

**PCT**

**INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY**  
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>A41147M</b>	<b>FOR FURTHER ACTION</b>		See Form PCT/IPEA/416
International application No. <b>PCT/JP2004/003578</b>	International filing date (day/month/year) <b>17.03.2004</b>	Priority date (day/month/year) <b>20.03.2003</b>	
International Patent Classification (IPC) or national classification and IPC			
Applicant <b>RESEARCH FOUNDATION ITSUU LABORATORY</b>			

<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>4</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>																									
<p>4. This report contains indications relating to the following items:</p> <table border="0"> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. I</td> <td>Basis of the report</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>		<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2004/003578

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of:
- ☐ international search (Rule 12.3 and 23.1(b))
- ☐ publication of the international application (Rule 12.4)
- ☐ international preliminary examination (Rule 55.2 and/or 55.3)
2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:
- ☒ the international application as originally filed/furnished
- ☐ the description:
- pages \_\_\_\_\_ as originally filed/furnished
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☐ the claims:
- nos. \_\_\_\_\_ as originally filed/furnished
- nos.\* \_\_\_\_\_ as amended (together with any statement) under Article 19
- nos.\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- nos.\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☐ the drawings:
- sheets \_\_\_\_\_ as originally filed/furnished
- sheets\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- sheets\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to sequence listing (*specify*): \_\_\_\_\_
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to sequence listing (*specify*): \_\_\_\_\_

\* If item 4 applies, some or all of those sheets may be marked "superseded."

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2004/003578

Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement		
1. Statement			
Novelty (N)	Claims	1-9	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-9	NO
Industrial applicability (IA)	Claims	1-9	YES
	Claims		NO
2. Citations and explanations (Rule 70.7)			
Document 1: Diabetes (2002), Vol. 51, No. 3, pages 718 to 723			
Document 2: Mol Genet Metab. (2001), Vol. 74, No. 3, pages 362 to 369			
Document 3: Am. J. Respir. Cell Mol. Biol. (2001), Vol. 25, No. 6, pages 744 to 750			
Document 4: Blood (1998), Vol. 91, No. 2, pages 724 and 725			
Document 5: J. Cell Biol. (2000), Vol. 148, No. 4, pages 679 to 690			
Document 6: EP 1285961 A1			
Document 7: Mol Cell Biol. (1995), Vol. 15, No. 7, pages 3540 to 3551			
Claims 1 to 6			
Documents 1 and 2 respectively indicate that LG100268, which is a retinoic acid X receptor ligand, and an agonist of said receptor, differentiate an anaplastic cell such as the fat cell precursor cell of vertebrate animals.			
Documents 1 and 2 do not go as far as indicating that organs and tissue are formed, but it would be easy for a person skilled in the art to conceive of using a			

Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
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reagent having a differentiation-inducing capacity capable of differentiation to attempt to form organs and/or tissue.

It would therefore be easy for a person skilled in the art to constitute the invention set forth in claims 1 to 6 in the light of the inventions set forth in documents 1 and 2.

Claims 7 to 9

Documents 3 to 5 indicate that agonists and antagonists which are retinoic acid derivatives that bind to retinoic acid receptor subtype  $\alpha$  differentiate anaplastic cells of vertebrate animals.

These documents differ from the invention set forth in claim 7 in that said documents do not go as far as indicating that a spleen is formed, and that the formation takes place in the presence of activin, but document 6 indicates that activin and retinoic acid are used in differentiating the anaplastic cells of a vertebrate animal to the spleen. It would therefore be easy for a person skilled in the art to use the retinoic acid derivative set forth in documents 3 to 5 as an alternative to the retinoic acid set forth in document 6 to constitute the invention set forth in claims 7 and 9 of this application.

In addition, the specific retinoic acid receptor ligand (Am80) set forth in claim 8 is known as a retinoic acid receptor subtype  $\alpha$  ligand (document 7, table 1), and it would not be particularly difficult for a person skilled in the art to employ said ligand.